

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference ITR0064Y	FOR FURTHER ACTION		See item 4 below
International application No. PCT/EP2005/000559	International filing date (<i>day/month/year</i>) 18 January 2005 (18.01.2005)	Priority date (<i>day/month/year</i>) 21 January 2004 (21.01.2004)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ANGELETTI SPA			

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | |
|---|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> Box No. II | Priority |
| <input checked="" type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> Box No. VI | Certain documents cited |
| <input checked="" type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland		Date of issuance of this report 24 July 2006 (24.07.2006)
Facsimile No. +41 22 338 82 70		Authorized officer Agnes Wittmann-Regis
Form PCT/IB/373 (January 2004)		e-mail: pt06@wipo.int

PATENT COOPERATION TREATY

REC'D 28 JUN 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

4/8

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/000559

International filing date (day/month/year)
18.01.2005

Priority date (day/month/year)
21.01.2004

International Patent Classification (IPC) or both national classification and IPC
C12N15/11, A61K31/713, C12Q1/68

Applicant
ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Authorized Officer

Surdej, P

Telephone No. +49 89 2399-7334



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000559

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☒ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000559

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1, 2, 4, 9-16

because:

- ☒ the said international application, or the said claims Nos. 1, 2, 4, 9-13 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☒ the claims, or said claims Nos. 1-2, 4, 9-16 (all partially) are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000559

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-17
	No: Claims	
Inventive step (IS)	Yes: Claims	17
	No: Claims	1-16
Industrial applicability (IA)	Yes: Claims	3, 5-8, 14-17
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VII Certain defects in the International application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Reference is made to the following documents:

- D1: GAO LIN ET AL: "Cloning and functional characterization of HDAC11, a novel member of the human histone deacetylase family." THE JOURNAL OF BIOLOGICAL CHEMISTRY. 12 JUL 2002, vol. 277, no. 28, 12 July 2002 (2002-07-12), pages 25748-25755, XP002324623 ISSN: 0021-9258
- D2: WO 03/068961 A (AXORDIA LIMITED; ANDREWS, PETER; WALSH, JAMES; GOKHALE, PAUL) 21 August 2003 (2003-08-21)
- D3: KRÄMER O H ET AL: "Histone deacetylase as a therapeutic target." TRENDS IN ENDOCRINOLOGY AND METABOLISM: TEM. SEP 2001, vol. 12, no. 7, September 2001 (2001-09), pages 294-300, XP002329890 ISSN: 1043-2760
- D4: ARENZ CHRISTOPH ET AL: "RNA interference: from an ancient mechanism to a state of the art therapeutic application?" DIE NATURWISSENSCHAFTEN. AUG 2003, vol. 90, no. 8, August 2003 (2003-08), pages 345-359, XP002324624 ISSN: 0028-1042
- D5: ACHENBACH TATJANA V ET AL: "Oligonucleotide-based knockdown technologies: antisense versus RNA interference." CHEMBIOCHEM : A EUROPEAN JOURNAL OF CHEMICAL BIOLOGY. 6 OCT 2003, vol. 4, no. 10, 6 October 2003 (2003-10-06), pages 928-935, XP002324625 ISSN: 1439-4227
- D6: LU PATRICK Y ET AL: "siRNA-mediated antitumorigenesis for drug target validation and therapeutics." CURRENT OPINION IN MOLECULAR THERAPEUTICS. JUN 2003, vol. 5, no. 3, June 2003 (2003-06), pages 225-234, XP009037747 ISSN: 1464-8431
- D7: KITTLER RALF ET AL: "RNA interference: gene silencing in the fast lane." SEMINARS IN CANCER BIOLOGY. AUG 2003, vol. 13, no. 4, August 2003 (2003-08), pages 259-265, XP002266372 ISSN: 1044-579X
- D8: WO 2004/094636 A (GALAPAGOS GENOMICS N.V; ARTS, GERARDUS, JOHANNES, FRANCISCUS; VAN DER) 4 November 2004 (2004-11-04)

Introduction

The application discloses a method of treating a subject suffering from a cell-proliferative disorder with a therapeutically effective amount of an HDAC 11 inhibitor. Method of treating of antisense strand sequence of a HDAC11 capable of producing a mammalian

HDAC11 protein in a cell. A short interfering nucleic acid (siRNA) molecule that down regulates expression of a mammalian HDAC 11 gene by RNA interference and uses thereof such as therapeutic use in cell-proliferative disorder. SEQ ID NO:1 is the DNA of HDAC11 and SEQ ID No.3-10 are sense and antisense oligonucleotides. The application draws priority from one priority document which has the priority date 21 January 2004 (P1).

Re Item II

Priority

1. Not all the priority documents were available at the time of the establishment of the present opinion which consequently has been established assuming that all the claims are entitled to the earliest claimed priority. Should, however, the priority be invalid, the Applicant is informed that documents D8 would be detrimental to the novelty and/or inventivity of the claimed subject-matter.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. No search report was established on the subject-matter of claims 1-2, 4, 12-16 (all partially)(Rule 66.1(e) PCT) as far as concerning HDAC inhibitors other than siRNA. Therefore, only the subject-matter of claims 1-2, 4, 12-16 (all partially) concerning siRNA is considered herein.
3. Claims 1-2, 4, 9-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement Article 35(2) PCT with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty and inventive step (Art. 33(1)-(3) PCT)

4. The subject-matter of claims 1-16 is new but not inventive. D1 discloses the cloning and characterization of a human cDNA that belongs to the histone deacetylase family designated as HDAC11 which displays a histone deacetylase activity in vitro (abstract, page 25753, left-hand column, last §, page 25754, right-hand column). Furthermore, HDAC11's enzymatic activity is inhibited by trapoxin, a known histone deacetylase inhibitor. The difference of the application with D1 is the nature of the inhibitor. Therefore the problem can be defined as the provision of further inhibitors of the expression of HDAC11. However, such problem is solved only by a very limited number of compounds disclosed in the application, namely, the siRNAs of claim 17. Therefore, the skilled person is left with an undue burden to achieve the effect wished over the whole scope of said claims. In consequence, no inventive step can be acknowledged for said claims.
6. Limited to the compounds of claim 17, the subject-matter of the application is considered to be inventive.

Industrial Applicability (Art. 33. (1) and (4) PCT)

5. For the assessment of the present claims 1-2, 4, 9-13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
D8: WO 04/094636	04/11/04	24/04/03	24/03/04

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/000559

6. The Applicant's attention is drawn to the fact that D8 will be considered as prior art in some PCT Contracting States. The EPO, for example, will consider D8 as prejudicial to the novelty of the subject-matter of the present application (Article 54(3) and (4) EPC) insofar as the same Designated Contracting States are concerned.

PATENT COOPERATION TREATY

REC'D 28 JUN 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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4/8

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/000559

International filing date (day/month/year)
18.01.2005

Priority date (day/month/year)
21.01.2004

International Patent Classification (IPC) or both national classification and IPC
C12N15/11, A61K31/713, C12Q1/68

Applicant
ISTITUTO DI RICERCHE DI BIOLOGIA MOLECOLARE P ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1 (a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000559

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☒ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000559

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1, 2, 4, 9-16

because:

- ☒ the said international application, or the said claims Nos. 1, 2, 4, 9-13 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☒ the claims, or said claims Nos. 1-2, 4, 9-16 (all partially) are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000559

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-17
	No: Claims	
Inventive step (IS)	Yes: Claims	17
	No: Claims	1-16
Industrial applicability (IA)	Yes: Claims	3, 5-8, 14-17
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Reference is made to the following documents:

- D1: GAO LIN ET AL: "Cloning and functional characterization of HDAC11, a novel member of the human histone deacetylase family." THE JOURNAL OF BIOLOGICAL CHEMISTRY. 12 JUL 2002, vol. 277, no. 28, 12 July 2002 (2002-07-12), pages 25748-25755, XP002324623 ISSN: 0021-9258
- D2: WO 03/068961 A (AXORDIA LIMITED; ANDREWS, PETER; WALSH, JAMES; GOKHALE, PAUL) 21 August 2003 (2003-08-21)
- D3: KRÄMER O H ET AL: "Histone deacetylase as a therapeutic target." TRENDS. IN ENDOCRINOLOGY AND METABOLISM: TEM. SEP 2001, vol. 12, no. 7, September 2001 (2001-09), pages 294-300, XP002329890 ISSN: 1043-2760
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- D5: ACHENBACH TATJANA V ET AL: "Oligonucleotide-based knockdown technologies: antisense versus RNA interference." CHEMBIOCHEM : A EUROPEAN JOURNAL OF CHEMICAL BIOLOGY. 6 OCT 2003, vol. 4, no. 10, 6 October 2003 (2003-10-06), pages 928-935, XP002324625 ISSN: 1439-4227
- D6: LU PATRICK Y ET AL: "siRNA-mediated antitumorigenesis for drug target validation and therapeutics." CURRENT OPINION IN MOLECULAR THERAPEUTICS. JUN 2003, vol. 5, no. 3, June 2003 (2003-06), pages 225-234, XP009037747 ISSN: 1464-8431
- D7: KITTLER RALF ET AL: "RNA interference: gene silencing in the fast lane." SEMINARS IN CANCER BIOLOGY. AUG 2003, vol. 13, no. 4, August 2003 (2003-08), pages 259-265, XP002266372 ISSN: 1044-579X
- D8: WO 2004/094636 A (GALAPAGOS GENOMICS N.V; ARTS, GERARDUS, JOHANNES, FRANCISCUS; VAN DER) 4 November 2004 (2004-11-04)

Introduction

The application discloses a method of treating a subject suffering from a cell-proliferative disorder with a therapeutically effective amount of an HDAC 11 inhibitor. Method of treating of antisense strand sequence of a HDAC11 capable of producing a mammalian

HDAC11 protein in a cell. A short interfering nucleic acid (siRNA) molecule that down regulates expression of a mammalian HDAC 11 gene by RNA interference and uses thereof such as therapeutic use in cell-proliferative disorder. SEQ ID NO:1 is the DNA of HDAC11 and SEQ ID No.3-10 are sense and antisense oligonucleotides. The application draws priority from one priority document which has the priority date 21 January 2004 (P1).

Re Item II

Priority

1. Not all the priority documents were available at the time of the establishment of the present opinion which consequently has been established assuming that all the claims are entitled to the earliest claimed priority. Should, however, the priority be invalid, the Applicant is informed that documents D8 would be detrimental to the novelty and/or inventivity of the claimed subject-matter.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. No search report was established on the subject-matter of claims 1-2, 4, 12-16 (all partially)(Rule 66.1(e) PCT) as far as concerning HDAC inhibitors other than siRNA. Therefore, only the subject-matter of claims 1-2, 4, 12-16 (all partially) concerning siRNA is considered herein.
3. Claims 1-2, 4, 9-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement Article 35(2) PCT with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty and inventive step (Art. 33(1)-(3) PCT)

4. The subject-matter of claims 1-16 is new but not inventive. D1 discloses the cloning and characterization of a human cDNA that belongs to the histone deacetylase family designated as HDAC11 which displays a histone deacetylase activity in vitro (abstract, page 25753, left-hand column, last §, page 25754, right-hand column). Furthermore, HDAC11's enzymatic activity is inhibited by trapoxin, a known histone deacetylase inhibitor. The difference of the application with D1 is the nature of the inhibitor. Therefore the problem can be defined as the provision of further inhibitors of the expression of HDAC11. However, such problem is solved only by a very limited number of compounds disclosed in the application, namely, the siRNAs of claim 17. Therefore, the skilled person is left with an undue burden to achieve the effect wished over the whole scope of said claims. In consequence, no inventive step can be acknowledged for said claims.
6. Limited to the compounds of claim 17, the subject-matter of the application is considered to be inventive.

Industrial Applicability (Art. 33. (1) and (4) PCT)

5. For the assessment of the present claims 1-2, 4, 9-13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
D8: WO 04/094636	04/11/04	24/04/03	24/03/04

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/000559

6. The Applicant's attention is drawn to the fact that D8 will be considered as prior art in some PCT Contracting States. The EPO, for example, will consider D8 as prejudicial to the novelty of the subject-matter of the present application (Article 54(3) and (4) EPC) insofar as the same Designated Contracting States are concerned.